REMARKS

This Reply is responsive to the Office Action dated October 12, 2001. Reconsideration of the subject application in light of the remarks and amendments presented herein is respectfully requested pursuant to 37 CFR §1.116.

Claims 1 and 33 were amended above to incorporate the limitations of claims 29 and 36, respectively, thereby incorporating reference to the specific growth factors in the independent claims. Claims 29 and 36 were therefore canceled. Claim 30 was amended to depend on claim 1 in view of the cancellation of claim 29. In addition, new claims 41 and 42 were added which are dependent on claims 32 and 38, respectively, and which specify that the feeder cells are transfected with one or more genes encoding the recited growth factors. Support for the new claims may be found at page 13, lines 10-12 of the specification. No new matter has been added.

Turning now to the Office Action, claims 1, 4, 5, 7, 8 and 29-40 remain rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for a method of culturing avian PGCs for at least 14 days in culture in media comprising LIF, bFGF, IGF and SCF in sufficient amounts, allegedly fails to provide enablement for culturing avian PGCs in media comprising "growth factors in amounts sufficient to maintain said PGCs for at least 14 days" as broadly as claimed. Essentially, the Examiner's bases for the rejection are that (1) the presence of LIF, bFGF, IGF and SCF is considered to be essential to maintain the PGCs in culture for at least 14 days and therefore must be included in claims 1, 4, 5, 7, 8, 31-35 and 37-40; and (2) claims 32 and 38 are not enabled because "the art at the time of filing did not teach feeder cells that produced growth factors in amounts sufficient to maintain PGCs for at least 14 days." Applicants respectfully repeat their traversal as to both grounds for the rejection.

Applicants respectfully reiterate that they were the first to achieve long term maintenance of avian PGCs in culture as admitted by the Office. Indeed, as confirmed by the Examiner in the Action dated October 12, 2001, the claims are free of the prior art without reference to any specific growth factor. Accordingly, Applicants are justifiably entitled to a claim of sufficient scope as to warrant their novel contribution to the field. The scope of the

claims may reach to the boundaries of the prior art providing there is sufficient support in the specification. Although the Examiner dismisses the issued patents noted in the previous Reply as being founded on different facts and circumstances, given the willingness of the Office to issue broad claims for similar pioneering, long-term culturing methods, it is inappropriate to require the limitation of the specific growth factors in the instant case to be read into the claims.

Nevertheless, in order to expedite an allowance of the present application, applicants have amended the independent claims to require exposure of the cells to the specifically disclosed growth factors. Accordingly, withdrawal of this ground for the rejection is respectfully requested. Applicants note that claims 29 and 36 referred specifically to the growth factors disclosed in the specification and yet they were included in the scope of the enablement rejection. Although these claims are now canceled, the rejection of these claims appears to have been made in error.

The Examiner also maintains the second grounds for the rejection under §112, first paragraph, alleging that claims 32 and 38 are not enabled because the specification does not teach any feeder cells that provide growth factors in amounts sufficient to maintain PGCs for at least 14 days. Applicants respectfully reiterate that it is disclosed in the specification that feeder cells could be readily modified to express exogenous growth factors using techniques that are well known in the art.

For instance, the specification discloses that "feeder cells may be transfected with genes encoding these growth factors, thereby eliminating the need for the exogenous addition of these factors during culturing . . . by placing these growth factor genes under control of constitutive promoter and also sequences that provide for the secretion thereof" (see page 13, lines 10-15). According to a review of the literature available at the time the present application was filed, it was known that feeder cells transfected with a membrane-bound form of SCF could be used in lieu of soluble SCF. See the attached abstracts by Slanicka et al. (May, 1998) and Durcova-Hills et al. (August, 1998). Therefore, those of skill in the art as of the time the application was filed would have known that one way to supply the disclosed growth factors would have been via transfection of feeder cells. In this regard, new claims 41

and 42 were added above that specify that the recited feeder cells are transfected with one or more genes encoding the recited growth factors.

Furthermore, it was well known prior to the identification of specific growth factors produced by feeder cells that non-transfected feeder cells could serve as a source of growth factors even absent transfection. For instance, according to the abstract by Shim and Anderson (February, 1998), growth factors provided by either a STO feeder layer or porcine PGCs themselves were sufficient to support in vitro survival of the PGCs. Also, according to De Felici and Pesce (1994), primordial germ cell adhesion to different cell monolayers was found to provide access for the PGCs to different cell survival molecules, including steel factor and LIF. In fact, as previously disclosed by Matsui et al. (Sept., 1992), membrane-bound LIF and steel factor contributed to the maintenance of murine PGCs in culture for at least 20 passages.

Thus, it was known prior to the present invention that feeder cells produce factors that promote the survival of PGCs in culture, and that those factors include membrane bound or secreted forms of growth factors. Applicants have identified a specific growth factor combination that will promote the maintenance of avian PGCs in the absence of a feeder layer, but that does not preclude the use of a feeder layer to provide such identified growth factors. Indeed, the use of feeder layers to provide necessary cell survival factors was well known; the present invention merely defines the factors that to be produced by such feeder cells.

In light of all these remarks, reconsideration and withdrawal of the §112, first rejection is respectfully requested.

Claims 1, 4, 5, 7, 8, 29-31, 33-37, 39 and 40 remain rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-12 of U.S. Patent No. 6,156,569. Applicants respectfully request that this obvious-type double patenting rejection be held in abeyance until the indication of allowable subject matter, as the nature of the claimed subject matter may change during prosecution. If, at the indication of allowable subject matter the Examiner still believes such a rejection to be appropriate, applicants will consider filing a terminal disclaimer.

This Reply is fully responsive to the Office Action dated October 12, 2001. Accordingly, a Notice of Allowance is next in order. If the Examiner has questions relating to the subject application or to this Reply, he is encouraged to contact the undersigned so that prosecution may be expedited.

Respectfully submitted,

PILLSBURY WINTHROP LLP

By: _____

Bonnie Weiss McLeod
Registration No. 43,255

Robin Teskin

1600 Tysons Boulevard
McLean, VA 22102
(703) 905-2000
(703) 905-2500 Facsimile

Date: January 14, 2002
Enclosure: Appendix
Reference Abstracts

APPENDIX: VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims

1. (Twice Amended) A method for culturing avian primordial germ cells comprising maintaining said avian primordial germ cells for periods of at least fourteen days in tissue culture comprising the following steps:

(i) isolating a pure population of primordial germ cells from a desired avian; and

(ii) [culturing] exposing said isolated, pure population of primordial germ cells (PGCs) [in a culture medium comprising] to at least the following growth factors in amounts sufficient to maintain said PGCs for at least fourteen days in culture:

(1) leukemia inhibitory factor (LIF),

(2) basic fibroblast growth factor (bFGF),

(3) stem cell factor (SCF), and

(4) insulin-like growth factor (IGF).

30. (Twice Amended) The method of claim [29] 1, wherein the minimum amounts of said growth factors are:

(i) 0.00625 U/μl LIF;

(ii) 0.25 pg/μl bFGF;

(iii) 0.5625 pg/μl SCF; and

(v) 4.0 pg/μl IGF.

33. (Amended) A culture consisting essentially of purified isolated avian PGCs [contained in a culture medium comprising] exposed to growth factors in amounts sufficient to maintain said PGCs for at least fourteen days in tissue culture, wherein said growth factors include at least the following:

(1) leukemia inhibitory factor (LIF),

(2) basic fibroblast growth factor (bFGF),

(3) stem cell factor, and

(4) insulin-like growth factor (IGF).